***600355** GeneTests, Links

# BACULOVIRAL IAP REPEAT-CONTAINING PROTEIN 1; BIRC1

***Alternative titles; symbols***

**NEURONAL APOPTOSIS INHIBITORY PROTEIN; NAIP**

Gene map locus 5q12.2-q13.3

## TEXT

In a search for the gene causing spinal muscular atrophy (SMA; 253300), Roy et al. (1995) isolated a gene on chromosome 5q13.1, of which the first 2 coding exons were deleted in approximately 67% of type I SMA chromosomes compared with 2% of non-SMA chromosomes. One model of SMA pathogenesis invokes an inappropriate persistence of motor neuron apoptosis, which is a normally occurring phenomenon in development. Consistent with this hypothesis, the novel gene was labeled 'neuronal apoptosis inhibitory protein' (NAIP) and its function was supported by the finding that it contains domains with sequence similarity to IAPs, baculovirus proteins that inhibit virally induced insect cell apoptosis. The presence of a variable number of copies of truncated and internally deleted versions of the NAIP gene (pseudogenes) was thought to be a possible factor in the genesis of SMA. This situation was compared to that of the genes on 6p that code for steroid 21-hydroxylase (CYP21) deficiency (201910); through the processes of unequal crossing-over or gene conversion, mutations in the functional CYP21 gene can result. Roy et al. (1995) raised the possibility that NAIP functions in concert with SMN (600354) mutations in causing spinal muscular atrophy.

Although NAIP deletions are more frequently observed in patients affected by the acute form of SMA, it is not possible to establish an unambiguous correlation between deletion size and clinical severity. Novelli et al. (1997) investigated the effects of gender on the association between NAIP gene deletion and disease severity. No significant relationship between deletion size and clinical phenotype was observed among male patients, whereas in females the absence of NAIP was strongly associated with a severe phenotype (p less than 0.0001). SMA I was found in 75.6% of females and only 52.5% of males lacking NAIP. These results provided a possible molecular explanation for the sex-dependent phenotypic variation observed in SMA patients.

DiDonato et al. (1997) mapped the mouse homolog of NAIP to chromosome 13 in a region

showing conserved synteny with human 5q13.

Liston et al. (1996) demonstrated that expression of NAIP in mammalian cells inhibits apoptosis induced by a variety of signals.

NAIP, HIAP1 (601721), HIAP2 (601712), XIAP (300079), BIRC5 (603352), and BIRC6 (605638) are members of the mammalian inhibitors of apoptosis family and contain an N-terminal domain with 1 to 3 imperfect repeats of an approximately 65-amino acid domain named the baculovirus IAP repeat (BIR) motif. Gotz et al. (2000) identified 6 mouse Naip genes which were expressed in a broad range of tissues. Using a neurite outgrowth assay in rat pheochromocytoma PC12 cells, they observed that Naip overexpression impaired nerve growth factor (NGF)-induced neurite outgrowth. The BIR motifs of Naip (residues 1-345) were not required for this effect. However, the BIR domains of Naip were essential to prevent apoptosis in PC12 cells after NGF deprivation or tumor necrosis factor-alpha receptor (TNFAR; 191190) stimulation. Expression of full-length but not BIR-deleted Naip protected against cell death. This correlated with reduced activity of the cell death effector protease, caspase-3 (600636), in lysates of Naip-PC12 cells. The authors hypothesized that dysregulation of cellular differentiation and/or caspase suppression may contribute to motoneuron dysfunction and cell death in spinal muscular atrophy where NAIP is mutated.

## ANIMAL MODEL

In inbred mouse strains, permissiveness to intracellular replication of Legionella pneumophila is controlled by a single locus (Lgn1), which maps to a region within distal chromosome 13 that contains multiple copies of the Birc1 gene. Genomic BAC clones from the critical interval were transferred into transgenic mice to complement functionally the Lgn1-associated susceptibility of A/J mice to L. pneumophila. Diez et al. (2003) found that 2 independent BAC clones that rescued susceptibility had an overlapping region of 56 kb in which the entire Lgn1 transcript must lie. The full-length transcript of Birc1e (also called Naip5) is coded in this region. The results indicated a role for Birc1e in macrophage resistance to L. pneumophila infection. BIRC1 proteins are members of the inhibitor of apoptosis protein (IAP) family, structurally defined by baculovirus inhibitor of apoptosis repeat (BIR) domains implicated in protein-protein interactions. An antiapoptotic effect of BIRC1 has been described. Induction of apoptosis seems to be important for pathogenesis of L. pneumophila in human macrophages in vitro.

## REFERENCES

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The gene for neuronal apoptosis inhibitory protein is partially deleted in individuals with spinal muscular atrophy. *Cell* 80: 167-178, 1995.
PubMed ID : 7813013

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| | 309 | NAIP |
| | 214338 | MONOCLONAL |
| S1 | 4 | NAIP AND MONOCLONAL |
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| S2 | 4 | RD (unique items) |

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| Set | Items | Description |
|---|---|---|
| S1 | 201 | NAIP |
| S2 | 0 | S1 AND MONOCLON? |

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Product Number:**N6648**

Product Name:**Anti-NAIP antibody produced in rabbit**



Product Information

Description
Certificate of Analysis
MSDS
Datasheet
Structure Image

Options

Print Preview
Bulk Quote
Ask A Scientist

**Synonyms:** MDL number: MFCD01322381

**Storage Temp:** -20°C

**Comments:**

Affinity isolated antibody, Lyophilized powder

Species reactivity: human

**Immunogen:** synthetic peptide corresponding to amino acids 473-490 of human NAIP (neuronal apoptosis inhibitory protein) sequence, conjugated to KLH.

**Physical form:** Lyophilized from a 0.2 µm filtered solution in phosphate buffered saline

| Extended specifications | |
|---|---|
| Application(s) | |
| Immunoblotting | 10 µg/mL |

**Components:**

**Related Product(s):**

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25 The neuronal apoptosis inhibitory protein (**NAIP**) is a membrane-associated cytoplasmic protein in rabbit brain.

**T.A. Lynch and G.E. Morris**

*MRIC Biochemistry Group, North East Wales Institute, Wrexham LL11 2AW, UK.*

The Neuronal Apoptosis Inhibitory Protein (**NAIP**) gene was originally identified as a candidate gene for Spinal Muscular Atrophy (SMA). This disease is characterized by motor neuron degeneration, with evidence for an apoptotic mechanism. **NAIP** shares significant homology with two baculoviral inhibitor of apoptosis proteins, Cp-IAP and Op-IAP.

We have produced a panel of three **monoclonal** antibodies against a region of **NAIP** containing the baculovirus inhibitor of apoptosis repeats (BIRs). The antibodies recognized a protein of the predicted size (150kDa) in all brain regions tested and at lower levels in spinal cord and peripheral nerve. **NAIP** was undetectable in liver, heart and skeletal muscle. Immunohistochemistry of rabbit brain showed **NAIP** expression in the cytoplasm of neuronal cells, especially Purkinje neurons of the cerebellum and their dendritic processes. Subcellular fractionation of rabbit brain showed that the 150kDa **NAIP** protein sediments in heavy and light membrane fractions and is extractable with non-ionic detergent. The results suggest that **NAIP** is associated with internal membranes of the endoplasmic reticulum via a transmembrane sequence (aa 479-496). The N-terminal region, containing BIR domains and nucleotide-binding site, projects into the cytoplasm.

Supported by the Muscular Dystrophy Association (USA).

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# ProductInformation

**ANTI-NAIP**
Developed in Rabbit
Affinity Isolated Antibody

Product Number **N 6648**

**Product Description**
Anti-NAIP is developed in rabbit using a synthetic peptide conjugated to KLH as immunogen. This peptide corresponds to amino acids 473-490 (YLSLSSTRPDE-GLASIIC) of human NAIP. This antibody is affinity-purified human NAIP using peptide affinity chrom-atography.

Anti-NAIP detects human NAIP in extracts from *Sf* 21 insect cells expressing recombinant human NAIP by immunoblotting.

NAIP (neuronal apoptosis inhibitor protein) is a member of the IAPs (inhibitor of apoptosis proteins) that function in cell death pathways to inhibit programmed cell death.[1] Human NAIP has a calculated molecular mass of approximately 140 kDa. The IAPs share one to three copies of an approximately 70 amino acid sequence motif, BIR (baculovirus IAP repeat).[2] These BIR regions promote protein-protein interactions with caspases as well as with members of the TRAF family of signal molecules.[3]

The first human IAP identified was NAIP, discovered based on its association with a neurodegenerative disorder. Mutations and deletions in the NAIP gene locus is a contributing factor in spinal muscular atrophy.[4] Co-expression of NAIP and hippocalcin protects neurons against calcium-induced cell death in caspase-3-activated and non-activated pathways.[5] NAIP is strongly expressed in anterior horn and motor cortex neurons of the normal brain. It is also found in human fetal neurons and in adult choroid plexus cells.[6]

**Reagent**
Anti-XIAP is supplied as 100 µg of antibody lyophilized from a 0.2 µm filtered solution in phosphate buffered saline.

**Preparation Instructions**
To one vial of lyophilized powder, add 0.1 ml of 0.2 µm-filtered solution of phosphate-buffered saline (PBS) containing 0.02% sodium azide to produce a 1.0 µg/ml stock solution of antibody.

**Storage/Stability**
Prior to reconstitution, store at -20° C. The re-constituted product may be stored at 2-8° C for at least one month. For prolonged storage, freeze in working aliquots at -20° C. Avoid repeated freezing and thawing.

**Product Profile**
The recommended working concentration is 1.0 µg/ml for immunoblotting using extracts from *Sf* 21 cells expressing human NAIP by chemiluminescent detection. The ability of the antibody to blot endogenous NAIP in cell extracts is not known.

Note: In order to obtain best results in different techniques and preparations we recommend determining optimal working dilutions by titration.

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